VOLUME 3

Study Title

Additional Information to Fulfill 40 CFR §26.1303 for the study:

Evaluation of the Efficacy of Personal Repellents Against Mosquitoes in the Laboratory

Supporting

***Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect* Repellent (EPA Reg. No. 806-29), *Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect Repellent Towelettes* (EPA Reg. No. 806-30), and *Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect Repellent Spray* (EPA Reg. No. 806-31)**

Data Requirement

Compilation of Information fulfilling 40 CFR §26.1303

Authors

Micah Reynolds, B.S.
J. Michael Kelley, Ph.D.

Compiled by

toXcel, LLC
7140 Heritage Village Plaza
Gainesville, VA 20155

Completed On

April 8, 2008

Project ID

Protocol ID: G0590607001A117
Project No. 0607-059-0157

Sponsor

Avon Products, Inc.
1251 Avenue of the Americas
New York, NY 10020

CONFIDENTIALITY STATEMENT

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA section 10(d)(1)(A), (B), or (C).

Company: Avon Products, Inc.

Company Agent: _____ Date: 4/9/08

J. Michael Kelley, Ph.D.
Vice President
toXcel, LLC
Authorized Representative of Avon Products, Inc.

NOTICE

This report is the property of Avon Products, Inc. and, as such, is considered to be confidential for all purposes other than compliance with FIFRA Section 10. Submission of this report in compliance with FIFRA does not constitute a waiver of any right of confidentiality that may exist under any other statute or in any other country.

GOOD LABORATORY PRACTICE STATEMENT

The enclosed compilation of information was not conducted according to the requirements of the Good Laboratory Practice regulations (40 CFR part 160).

Sponsor/Submitter: _____ Date: 4/9/08

J. Michael Kelley, Ph.D.
Vice President
toXcel, LLC
Authorized Representative of Avon Products, Inc.

Study Director: _____ Date: 4/8/2008

Micah Reynolds, B.S.
Associate Scientist
toXcel, LLC

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§ 26.1303 Submission of Completed Human Research for EPA Review

Any person who submits to EPA data derived from human research covered by this subpart shall provide at the time of submission information concerning the ethical conduct of such research. To the extent available to the submitter and not previously provided to EPA, such information should include:

	Requirement		Y/N	Comments/Page References
(a) Copies of all of the records relevant to the research specified by §26.1115(a) to be prepared and maintained by an IRB	§1115(a)(1): Copies of • all research proposals reviewed, • scientific evaluations, if any, that accompany the proposals, • approved sample consent documents, • progress reports submitted by investigators, and reports of injuries to subjects.		Y Y Y Y	Vol. 2 – pp. 10-50 of 98 Vol. 2 – pp. 1-79 of 98 Vol. 2 – pp. 54-64 of 98 Vol. 3 – p. 41 of 49 Investigator follow-up summary with study subjects
	§1115(a)(2): Minutes of IRB meetings which shall be in sufficient detail to show • attendance at the meetings; • actions taken by the IRB; • the vote on these actions including the number of • members voting for, against, and abstaining; • the basis for requiring changes in or disapproving research; • a written summary of the discussion of controverted issues and their resolution.		Y	Vol. 2 – p. 94 of 98 Vol. 3 – pp. 21-22,36-37 of 49
	§1115(a)(3): Records of continuing review activities.		Y	Vol. 3 – Investigator follow-up summary with study participants on p. 41 of 49.
	§1115(a)(4): Copies of all correspondence between the IRB and the investigators.		Y	Vol. 2 – p. 94 of 98 Vol. 3 – pp. 9,21-35 of 49
	§1115(a)(5): • A list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; • any employment or other relationship between each member and the institution, for example, full-time employee, a member of governing panel or board, stockholder, paid or unpaid consultant.		Y	Vol. 3 – pp. 38-40 of 49
	§1115(a)(6): Written procedures for the IRB in the same detail as described in § 26.1108(a) and § 26.1108(b).		Y	Written SOPs for the IRB previously submitted to EPA. Remain unchanged.
	§1115(a)(7): Statements of significant new findings provided to subjects, as required by § 26.1116(b)(5).		Y	Vol. 3 – Investigator follow-up summary on p. 41 of 49. No significant new findings resulted from the study.
(b) Copies of all of the records relevant to the information identified in §26.1125(a)-(f)	§1125(a) A discussion of:	(1) The potential risks to human subjects;	Y	Vol. 2 – pp. 20-22 of 98
		(2) The measures proposed to minimize risks to the human subjects;	Y	Vol. 2 – pp. 20-22 of 98
		(3): The nature and magnitude of all expected benefits of such research, and to whom they would accrue;	Y	Vol. 2 – p. 22 of 98
		(4) Alternative means of obtaining information comparable to what would be collected through the proposed research; and	Y	Vol. 2 – p. 17 of 98
		(5) The balance of risks and benefits of the proposed research.	Y	Vol. 2 – pp. 22-23 of 98
	§1125(b): All information for subjects and written informed consent agreements as originally provided to the IRB, and as approved by the IRB.		Y	Vol. 2 – pp. 54-64 of 98 Vol. 3 – pp. 11-20 of 49
	§1125(c): Information about how subjects will be recruited, including any advertisements proposed to be used.		Y	Vol. 2 – pp. 14-15,23-25 of 98
	§1125(d): A description of the circumstances and methods proposed for presenting information to potential human subjects for the purpose of obtaining their informed consent.		Y	Vol. 2 – pp. 14-15,23-25 of 98
	§1125(e): All correspondence between the IRB and the investigators or sponsors.		Y	Vol. 2 – p. 94 of 98 Vol. 3 – pp. 9,21-35 of 49
	§1125(f): Official notification to the sponsor or investigator, in accordance with the requirements of this subpart, that research involving human subjects has been reviewed and approved by an IRB.		Y	Vol. 2 – p. 94 of 98 Vol. 3 – pp. 21-22,36-37 of 49
(c) Copies of sample records used to document informed consent as specified by §26.1117, but not identifying any subjects of the research			Y	Vol. 2 – Approved ICD on pp. 54-64 of 98. Subject initials/code numbers identified on raw data collection sheets on pp. 66-72 of 98.
(d) If any of the information listed in paragraphs (a) through (c) of this section is not provided, the person shall describe the efforts made to obtain the information.			N/A	Page references provided for information listed in (a) thru (c) above.

Reference Document of Major Revisions to the Study Protocol and Informed Consent Document Since the October 2007 HSRB meeting

Review of ICR Mosquito Laboratory Protocol (A117)

The protocol was found to be scientifically and ethically acceptable provided that the requested changes are made and accepted by the Essex IRB prior to initiating the study. It was specifically noted at the conclusion of the HSRB meeting that a revised statistical analysis plan would need to be submitted to the Agency for review.

Revisions to the study protocol and informed consent document (ICD) were based on the Agency's science and ethics review as well as HSRB comments and recommendations. This document briefly summarizes Agency and HSRB recommendations and denotes the location(s) of major revisions undertaken on the protocol and ICD by citing page numbers, where appropriate, for easy reference to the changes made.

NOTE: It is important to identify that the cover letter and administrative materials (i.e. product label and EPA forms) compose **Volume 1** of this submission. The study protocol is contained in the investigator's final report (**Volume 2**) of this submission. The Essex IRB fully approved the revised protocol upon its review in February 2008 with no requested changes. In essence, this protocol represents the protocol as reviewed by the Essex IRB as well as the final protocol for the study. All page references to the protocol refer back to Volume 2. The revised ICD (version date February 8, 2008) that was initially reviewed by the Essex IRB in February 2008 is contained in this additional information supplement (**Volume 3**) on pages 11-20. The Essex IRB requested several changes to the ICD (changes identified in the correspondence section of this volume). The ICD was subsequently revised by ICR and approved by the Essex IRB. The final ICD (version date February 20, 2008) is included in the investigator's final report, and all page references to the ICD also refer back to Volume 2.

The following is a brief summary of the recommended changes to the protocol and ICD as a result of Agency and HSRB review from the October 2007 meeting. Page number references for the protocol (PCOL) and informed consent document (ICD) are noted parenthetically in bold font:

1) **Science Review by Agency (Kevin Sweeney/EPA)**
   A. Comments in Science Review
      - Justify why not using 200 mosquitoes per cage as recommended by EPA
        a. We informed the board we will use 200 mosquitoes **(PCOL changes throughout)**
      - Further explain statistical analysis especially how to calculate normality and how non-normal data will be analyzed. Need statistics for all contingencies (i.e. If no one drops out) **(PCOL pp. 28-35/98)**
      - Call endpoint "Complete Protection Time" instead of "Protection Time" **(PCOL changes throughout)**
      - Add data collection form for determination of subject attractancy **(PCOL p. 38/98)**

- Append protocol to include EPA-registered product labels **(PCOL pp. 41-50/98)**

2) **Ethics Review by the Agency (John Carley/EPA)**
   A. Required Documentation not provided
      - Discussion of nature and magnitude of all expected benefits as required by 40CFR26.1125(a)(3). **(PCOL p. 22/98, ICD p. 62/98)**
      - Discussion of the balance of risks and benefits as required by 40CFR26.1125(a)(5). **(PCOL pp. 22-23/98)**
      - Description of informed consent process. **(PCOL p. 14-15,23-25/98)**
   B. Comments in Agency's Ethics Review of September 24, 2007
      - Discussion of benefits needs to be rewritten to focus on protection from WNV and not generation of new products. Also revise risk/benefit section to explain Sponsor is primary beneficiary and insect repellant users are indirect beneficiaries with improved protection from WNV. **(PCOL p. 22-23/98, ICD p. 62/98)**
      - Remove language that subjects are representative of repellant users **(PCOL/ICD changes throughout)**
      - Identified risk to the test materials is misleading. Protocol cites that active ingredient is classified as Tox. Cat. IV, but the actual compounds tested are Tox. Cat. III (806-29) and Tox. Cat. II (806-31) based on eye irritation. **(PCOL pp. 20-21/98, ICD pp. 60-61/98)**
      - No clear reason to cap participant age at 55 since disease is not a risk. **(PCOL p. 23/98, ICD p. 55/98)**
      - Eligibility criteria inappropriately defined in ICD. **(PCOL p. 23/98, ICD pp. 55-56/98)**
      - Discuss in consent documents the mosquitoes are known to carry disease vectors but since they are lab-reared they have no risk of carrying disease. **(ICD pp. 54,60/98)**
      - Clarify informed consent process. References to "study subjects" prior to the signing of the ICD is incorrect. Refer to as candidates, interested persons, or potential subjects. **(ICD changes throughout)**
      - Remove signature on data collection forms. **(PCOL pp. 38-40/98)**
      - Make the control subject selection description consistent in different parts. **(PCOL p. 23-26/98, ICD pp. 57-58/98)**

3) **Board Review of Science and Ethical Issues**
   A. Ethics review
      a. Recommends clarifying risk of test materials as opposed to the AI. **(PCOL p. 20-21/98, ICD pp. 60-61/98)**
      b. Recommends putting reference to WNV in ICD but clarify that it is not a risk in this study. **(ICD pp. 54,60/98)**
      c. Provide further description of the subject recruitment process **(PCOL p. 14-15,23-25/98)**
      d. Measure of subject attractancy must be added to the ICD. **(PCOL p. 15,26/98, ICD pp. 57-58/98)**
      e. Amend the benefits section to indicate that primary benefit is to add label claims of repellency of WNV vectors, not bringing new product to market. **(PCOL p. 22-23/98, ICD p. 62/98)**
      f. Cites that primary risk is not from test material or mosquito bites, but from test environment (high temperature/humidity). Recommends citing this as potential risk in ICD. **(PCOL p. 20/98, ICD p. 59/98)**

g. Provide discussion of medical monitoring/emergency response plan in ICD and protocol **(PCOL p. 22/98, ICD p. 61/98)**

4) Discussions and Recommendations

A. Minor New Issues

- Extended test duration to 10 hours. **(PCOL pp. 18,27-29/98, ICD p. 59,61/98)**
- Age cap increased to 70 years of age due to no restrictions resulting from arthropod-borne diseases. **(PCOL p. 18,23/98, ICD p. 55/98)**
- Revised statistical analysis plan. **(PCOL pp. 28-35/98)**

ICR | *Independent Laboratory*
Pesticide Efficacy Testing
Regulatory Services

February 14, 2008

Chairman
Essex Institutional Review Board, Inc.
121 Main Street
Lebanon, NJ 08833-2162

Protocol # G0590607001A117 **ICR Project # 0607-059-0157**
Version Date February 8, 2008

Dear Dr. Lambert:

Please find enclosed the following protocol and associated Informed Consent Form: Protocol # G0590607001A117 ICR Project # 0607-059-0157 Version Date February 8, 2008.

Protocol G0590607001A117 version date June 12, 2007 was approved by Essex Institutional Review Board August 6, 2007. This protocol was amended as per changes requested by the EPA and the HSRB during the October 2007 review. These changes are incorporated in the protocol with version date February 8, 2008.

We are requesting an amendment review for this project. The proposed date that the study will be conducted is **February(last week) or early March 2008**, so we respectfully request that we receive your approval prior to this date. We would like these documents sent to us by **Federal Express Overnight**, so please charge the delivery to our FedEx account number 1028-0348-5.

We also request a copy of the minutes of any followup meeting that the IRB has that pertain to this study, so that we submit them to EPA's HSRB as required by the Final Rule.

We enclose the following documents to support our request:

We are enclosing the following documentation to support this request:
-Protocol (please return **one approved copy** to us)
-Informed Consent Form

Thank you for your attention, and please do not hesitate to contact me by telephone at 410-747-4500, by fax at 410-747-4928, or email address nspero@icrlab.com if you have any questions.

Sincerely,

Niketas C. Spero
Principal Investigator

Enclosures

1330 Dillon Heights Avenue, Baltimore, MD 21228-1199 | tel 410.747.4500 | fax 410.747.4928 | web www.icrlab.com

ICR, INC
1330 Dillon Heights Avenue
Baltimore, MD 21228
Telephone: (410) 747-4500
Fax: (410) 747-4928

Protocol Amendment

Project Number:	0607-059-0157
Protocol Number:	G0590607001A117 Version Date February 8, 2008
	Amended as Version Date February 8, 2008
Sponsor:	Avon Products, Incorporated
Test Article(s):	TA# 1001108-030 (A)
	TA# 1004024-010 (B)
GLP Compliance:	40 CFR 160
Amendment:	Protocol G0590607001A117 version date June 12, 2007 was approved by Essex Institutional Review Board August 6, 2007. This protocol was amended as per changes requested by the EPA and the HSRB during the October 2007 review. These changes are incorporated in the protocol with version date February 8, 2008.

Impact On The Study: These changes improve the clarity of the protocol.

Submitted by: Nikita Chow Date 2-13-08

Acknowledged by QA: Date 2/13/08

PROTOCOL: EVALUATION OF THE EFFICACY OF PERSONAL REPELLENTS AGAINST MOSQUITOES IN THE LABORATORY

INFORMED CONSENT AUTHORIZATION TO PARTICIPATE IN AN ICR, INC. MOSQUITO REPELLENT EVALUATION IN THE LABORATORY

Principal Investigator: Niketas C Spero
Address: ICR, Inc. 1330 Dillon Heights Ave. Baltimore, MD
Telephone Number: 410-747-4500
24 Hour Emergency Number: 410-371-7223

Purpose of Study

We (ICR, Inc.) have been contracted by Avon Products, Inc. to conduct a research study in our laboratory on two mosquito repellent products containing the active ingredient picaridin, to find out how well they repel a species of mosquito that can carry West Nile Virus (WNV). The mosquitoes used in this study are laboratory-reared and disease-free. The repellent products to be tested are Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect Repellent and Avon Skin-So-Soft SSS Bug Guard Plus Picaridin Insect Repellent Spray.

This study will take place in the ICR, Inc. lab with mosquitoes confined in cages. This document will explain the study to you so that you can make a free choice whether or not to participate.

We will review this document with you to make sure you understand what would be expected of you if you participate, and to explain the risks you would face through your participation. Please ask us about anything you do not understand. If you have come into our office to review the document, you may take it home with you if you need more time to think about whether to participate.

We will apply the eligibility standards listed on the next page to determine if you qualify to participate in the study. If you qualify, we will ask you to consider signing this document to indicate your consent to participate. Your signing indicates your willingness to participate in this study, but you would still be free to withdraw from the study at any time, without having to give a reason.

Test subject's initials:.....

Date:.....

If you decide you would like to participate, initial each page of this form and sign the last page in the presence of someone on the ICR staff. The Principal Investigator will sign the form as well, and you will be given a copy with both signatures. We will notify you by phone within one week whether you have been selected for the study.

Eligibility for the Study

To participate in this study you must meet the following conditions:

- Sex: No exclusions
- Age: You must be at least 18 and not over 70
- Race: No exclusions
- Health: Must consider yourself to be in good health.
- Literacy: You must be able to read, speak, and understand English
- You must be attractive to mosquitoes, as evidenced by at least 5 landings of caged mosquitoes on your untreated forearm within one minute.
- You must not be pregnant or breastfeeding. If you are female, you will be required to perform an over-the-counter urine pregnancy test on the morning of the study. ICR will provide the test kit, and a female ICR staff member will verify the results. ICR will keep the results of the pregnancy test confidential from everyone except you and the Principal Investigator.
- You must not be an employee or a relative of an employee of ICR Inc., Avon Products, Inc., toXcel, LLC, or any other party with an interest in this research.
- You must have no known sensitivity to mosquito bites, to insect repellents, or to skin care products

If you choose to participate in this study and are selected to be a study subject, you must also agree:

- To follow the directions of the Principal Investigator and other ICR staff.

Test subject's initials:.....

Date:.....

- Not to use tobacco, alcohol, or any scented cosmetic products after 8 p.m. the night before study, and on the day of the study until it is concluded.

- To wear proper protective clothing on the day of the study: blue jeans or other sturdy trousers, heavy socks, long sleeve shirts, and gloves. Gloves will be provided by ICR.

Laboratory Repellent Phase Summary

Thirteen subjects will participate in this one-day laboratory study over a period of about 11 hours. One of you will be selected by lot to serve as the "control subject", and will not be treated with the test repellents. The other 12 subjects will be "treated subjects", and will be treated with both of the repellents, one on each forearm.

Every 30 minutes during the test, the untreated control subject will put one untreated forearm into each test cage containing 200 mosquitoes for one minute. If fewer than 5 mosquitoes land within one minute, 200 more mosquitoes will be added to each cage to ensure enough activity for a valid test.

After the untreated control subject has verified adequate mosquito activity, the 12 treated subjects will carefully put both forearms into their assigned cage with the mosquitoes for five minutes.

This pattern will be continued every half hour until you receive either two mosquito bites on the same arm in the same 5-minute exposure period, or one bite in each of two consecutive 5-minute exposure periods, or until ten hours after your treatment, whichever happens first.

Procedures
On the day of the study, before the test begins:

- We will review this document with you and answer any additional questions you may have since you have signed it.

- You will wash your arms with unscented Neutrogena soap.

Test subject's initials:.....

Date:.....

- We will measure and mark a 3 to 5 inch wide test area around each of your forearms as described in detail below.

- After we have measured your arms and protected the skin outside the test area we will determine your attractiveness to mosquitoes as described below.

- Unless you are selected as the untreated control subject, we will treat both your arms with test repellents and the study will begin.

Here is how that will work in detail:

Laboratory Study Details

1. One of you will be selected by lot to be the untreated control subject.

2. We will measure the distance around your arm at the wrist and the elbow, and calculate how wide a band is needed for the standard test area on your arm. This 3 - 5 inch wide band will be wider on thinner arms; narrower on bigger arms. We will then use a felt-tip pen to mark the location of the band around each of your forearms. The control subject will be measured and marked on only one forearm.

3. We will protect the skin above and below the marked test area from mosquito bites with multiple layers of elastic bandages and or Velcro® straps held in place with adhesive tape.

4. We will verify that you are attractive to mosquitoes. You will put one forearm into a test cage containing 200 mosquitoes, and we will count the number of mosquitoes landing on your arm. We will show you how to shake landing mosquitoes off your arm before they have a chance to bite you. If 5 mosquitoes land on your arm in a minute or less you will qualify as "attractive". You will then repeat the same procedure with your other arm. If you are not attractive after one attempt, you may repeat the process a second time. If you fail to attract mosquitoes in two trials you will not be eligible to participate in the study.

5. If you are a treated subject, we will apply one of the repellents to the test area on each

of your forearms, using a syringe without the needle. The amount of repellent applied will be a standardized "typical consumer dose". If you are the untreated control subject, you will receive no treatment.

6. With a fingertip in a latex or vinyl glove we will spread the repellent evenly over the test areas. Once your arms have been treated, you must be careful not to rub them against anything, as this could rub off some of the test repellent and change the results of the study.

7. We will mark your bandages with a letter identifying the repellent applied to that arm. We will not identify the repellents to you.

8. You will go to the test laboratory and wait for your repellents to dry for about one-half hour. Then you will put on gloves to protect your hands from bites, ready for your first 5-minute exposure period of the day.

9. ICR staff will show you which cage to use. Treated subjects will work in pairs. When you see a mosquito land on your own or your partner's arm, notify ICR staff.

10. Every 30 minutes after the test begins, the untreated control subject will put one arm into each of the six test cages in turn, to verify mosquito activity. As soon as 5 mosquitoes land, the control subject will remove his or her arm from the cage. If fewer than 5 mosquitoes land on the control subject's arm within one minute, 200 fresh mosquitoes will be added to each cage. ICR staff will show the control subject how to shake landing mosquitoes off before they have time to bite. Nonetheless it is likely that the control subject will get some bites during the course of the study.

11. Every 30 minutes after the study begins, after the activity of the mosquitoes in their assigned cage has been verified, each pair of treated subjects will carefully put both their arms into the cage for 5 minutes. During the 5-minute exposure period we will count the number of mosquitoes (up to two) that bite the treated skin of either of your arms. When you receive two bites on the same arm in one exposure period, or one bite in each of two consecutive exposure periods, you will remove that arm from the cage and from the study. We will call this "breakdown", and once you reach breakdown on one of your arms you will no longer expose that arm for the rest of the

Test subject's initials:.....

Date:.....

day's study. You can then remove the bandages and tape from this arm, and scratch if you choose. Caladryl®, Calamine® lotion and rubbing alcohol will be provided to help stop the itching from bites you received. When you reach breakdown on both arms, you will have finished your part in the study and may go home.

12. After each 5-minute exposure period you may leave the insectary, but you must remain in the lab. You can go to the restroom if you need to, and the Study Director will call breaks every few hours. You may either bring your own lunch or pay to have lunch ordered.

13. After preparation and treatment of subjects, which will take about one hour, the day's study will include up to 20 5-minute exposure periods at 30 minute intervals over 10 hours. The study will end after 10 hours or when all treated test subjects have reached breakdown on both arms, whichever comes first.

Discomfort and Hazard

You will be exposed to four types of risk throughout the duration of this study:

1. Testing environment

The testing environment isn't hazardous, but it will be warm and humid and may be uncomfortable for some of you. The test exposures will take place in a room kept at a temperature between 70 and 85°F and at relative humidity between 70 and 85%, however, between 5-minute exposure periods, you will be able to rest in other more comfortable areas of the laboratory. ICR staff will be visually monitoring all subjects for any signs of a reaction to the elevated temperature and humidity of the insectary. If you become uncomfortable with the physical conditions, tell a member of the staff immediately.

2. Mosquito bites or probes

A bite occurs when a mosquito takes blood. A probe occurs when a mosquito pierces your skin but does not take blood. Similar irritation can result from either a bite or a probe. A mosquito bite or probe may cause itching, redness or swelling that will usually

disappear within a couple of days. In severe cases, a bite or probe may cause the development of large bumps on your skin, difficulty breathing, sweating and/or a rapid pulse. For some people this could be life-threatening.

All subjects will be exposed to mosquitoes for at least 2 minutes to verify attractiveness to mosquitoes. Although they try to shake landing mosquitoes off before they bite, they may be bitten.

Treated subjects will expose their forearms to mosquitoes for five minutes every half hour. Although they will not expose an arm further if they receive two bites on it in one exposure, or one bite in two consecutive exposure periods, they may receive more than two bites on each arm during the test. A bite which is not followed by another bite in the same or the next exposure will be disregarded. If you are a treated subject you will still need to receive at least two more bites on that arm to reach breakdown. The untreated control subject will be exposed to mosquitoes every half hour for up to one minute in each of six test cages. Although he or she will try to shake landing mosquitoes off before they bite, the control subject is likely to be bitten by some of them. We will minimize the irritation from bites or probes you receive by making Caladryl® or Calamine® lotion or rubbing alcohol available at the study site for your use after the study is completed.

3. Reaction to the test repellents

You may have a reaction to the test repellents.

The Sponsor has minimized this possibility by choosing an active ingredient (picaridin) that has demonstrated low acute oral, skin, and inhalation toxicity. The Environmental Protection Agency (EPA) has classified it as low toxicity for acute inhalation toxicity and primary skin irritation. EPA has classified the two test repellents as having low to mild toxicity based on eye irritation. For this reason it is important not to rub your eyes with your treated arms. The Sponsor has selected the non-repellent ingredients in the formulations because they are widely used in cosmetics and have a long history of safe use. ICR staff will be monitoring all subjects for any signs of a reaction to the test repellents. If you think you may be having such a reaction, tell a member of the staff immediately.

Test subject's initials:.....

Date:.....

4. Mosquito-borne disease

The species of mosquito being used in this study is capable of transmitting West Nile Virus in the field, but the mosquitoes used in this study will be laboratory-reared and disease-free, and they will never have had a blood meal. There is no risk of your contracting any mosquito-borne disease as a result of participation in this study.

Should you have any medical problems, we will have First- Aid qualified staff members, and First- Aid supplies on site. Throughout the course of the study, ICR staff will be visually monitoring all subjects for any signs of stress. We will have cell phones to make emergency calls if necessary. In the case of medical emergency, we will transport you to a selected local hospital at our expense. We will pay all of your medical bills for study-related illnesses and injuries. The Principal Investigator will contact you by telephone, two weeks after the study to ask if you have experienced any adverse effects. You should contact the Principal Investigator any time after the study if you experience any study-related adverse effects, either before or after this follow up call.

Financial Consideration

We will pay you $11/hour for the first 9 hours and $17.50 for each additional hour that you spend on the day of the study. The study will last about 10 hours with an additional hour of prep time (11 hours total), with a total payment of $134 paid to you. This payment will be mailed to you on the 15th or the last day of the month. If we ask you to drop out of the test, and you have complied with all of our requests, you will still receive full payment. If we ask you to drop out of the test because you have not followed all of our directions, or if you choose to drop out of the test, we will compensate you for time up to that point at the rate of $11 per hour.

Costs

There are no financial costs to you for participating in this study.

Test subject's initials:.....

Date:.....

Benefits

You will get no personal benefit from participating in this study. The sponsor, Avon Products, Inc. will gain the most direct benefit from the conduct of this study, which is expected to support additional marketing claims that the tested products effectively repel mosquitoes which can carry West Nile Virus, and increase potential sales.

Some benefit is also likely to result for society at large through demonstrating the effectiveness of these products in repelling a potentially important public health pest. This, in turn, will allow a greater selection of products to consumers that are effective in repelling mosquitoes that can transmit West Nile Virus.

Your Rights

We will give you an opportunity to discuss with us any aspects of this document or of the study it describes that are not clear to you, so that you fully understand the nature of the study, its purpose, and the procedures to be used, as well as the discomforts, and risks you may experience during or after the study. You are encouraged to ask questions at any time, before or after you consent to participate, and before, during, or after the study day itself. Your participation is entirely voluntary. You may decide not to take part in this study, and if you decide you would like to participate, you are free to change your mind at any time without having to explain, and without penalty or loss of benefits to which you may be otherwise entitled.

Alternative

The only alternative to participating is for you to decide not to.

Questions

If you have any questions about this study or suffer a reaction you think might be associated with the study, call us at 410-747-4500. If you have any questions about your rights as a research participant, or related concerns, you may contact the Essex Institutional Review Board (IRB), 121 Main Street, Lebanon, NJ 08833, telephone 908-236-7735. The Essex IRB is a committee that has reviewed this research project to help ensure that the rights and welfare of the

Test subject's initials:.....

Date:.....

participants are protected and that the study is designed and carried out ethically. Review of this study by the Essex IRB is not an endorsement of the study or its outcome.

Confidentiality

We and the sponsor or its agents may use the information obtained from your taking part in this test, and this information may become part of a report. We will keep your participation as confidential as possible referring to you in the study data and reports only by your initials or an arbitrary ICR identification. However, we cannot guarantee that your identity will be kept confidential; the sponsor, personnel associated with the study, a regulatory agency such as the Environmental Protection Agency (EPA), and the Essex Institutional Review Board (EIRB) all have a right to review your records.

Consent

I voluntarily agree to participate in this study. I will be given a copy of this signed form.
By signing this form I have not given up any of my legal rights.

_____

Signature of Subject Date Signature of Witness Date

_____

Printed Name of Subject Date

_____

Signature of Principal Investigator Date

Test subject's initials:.....

Date:.....

Nick Spero

From: "Karen Radcliffe" <kradcliffe@essexirb.com>
To: <nspero@ICRlab.com>
Sent: Tuesday, February 19, 2008 3:37 PM
Subject: Avon #G0590607001A117

Hi Nick:

The **Amended Protocol** (dated 2-8-08), reviewed by a full Board, was **approved on February 18, 2008.**

The **Revised Consent Form** (dated 2-8-08) was **conditionally approved** pending the following modifications:

Page 1:

- After **Principal Investigator** information and before **Purpose of Study** – Please add a new section title "**Introduction**" and the following paragraph: "You are being asked to participate in a research study. Before agreeing to participate in this study, it is important that you read this form. This form, called an informed consent document, describes the purpose, procedures, benefits, financial payment, risks and discomforts of the study. It also describes the alternative procedures that are available to you and your right not to participate or to withdraw from the study at any time. Please ask as many questions as you need to so that you can decide whether you want to be in the study. After reading this form and having all questions answered, if you decide to participate, you should return this consent form to the study doctor's office, sign this form on the last page, initial and date each prior page in the presence of the study staff. You may refuse to participate in this study and this decision will not be held against you."

Page 2:

- Under 1st paragraph, top of page, line 2 - Under 2nd paragraph, line 2 – Please delete the words "someone on" after the words "presence of".

Page 5:

- Under item 6, line 1 – Please replace the words "**in** a latex" with the words "**of** a latex".

Page 6:

- Under item 13, line 2 – Please replace the number "**20**" with the word "**twenty**".
- Under section **Discomfort and Hazard** - Please delete the sentence beginning with the words "You will be exposed to".

Page 7:

- Under 2nd paragraph, top of page, line 1 – Please replace the words "**All subjects**" with the word "**You**".
- Under 2nd paragraph, top of page, line 2 – Please replace the words "they bite, **they**" with the words "they bite, **you**".
- Under 3rd paragraph, line 5 – Please add a comma after the words "a treated subject".
- Under 3rd paragraph, line 11 – Please delete the word "your" after the words "the study site for".

Page 8:

- Under section **4. Mosquito-borne disease**, 2nd paragraph, line 1 - Please delete the comma after the words "staff members".
- Under section **4. Mosquito-borne disease**, 2nd paragraph, line 2 - Please delete the words "First-Aid-" after the word "and".
- Under section **Financial Consideration**, line 3 – Please add a period after the words "payment of $134" and then delete the words "paid to you."
- After section **Costs** – Please add a Blank Box with the words "This space intentionally left blank" in the center of the box. There may only be 1" or less of space between the last line of the last paragraph on the page and the footer. (Page 8 has 1-1/4" of space.)

Page 9:

- Under section **Benefits**, 1st paragraph, line 1 – Please delete the sentence beginning with the words "The

sponsor, Avon Products, Inc. will gain".

- Under section **Benefits**, 2nd paragraph, line 1 – Please replace the words "**is also likely to**" with the words "**may**".
- Under section **Benefits**, 2nd paragraph, line 2 – Please replace the words "**a potentially important public health pest.**" with the words "**a noxious pest.**"
- Under section **Alternative** – Please rewrite this sentence as follows: "**The only alternative is not to participate.**"
- After section **Alternative** - Please add a new section titled "**NEW INFORMATION**" and add the following paragraph: "You will be informed verbally or in writing of any significant new findings discovered during the course of this study which may influence your continued participation."
- After the new section **New Information** – Please add a new section titled **Voluntary Participation/Withdrawal** and add the following new paragraph: "You may be withdrawn from the study even if you want to continue. This could happen if (1) the study doctor believes it is in your best interest for you to stop being in the study, (2) or if you do not follow instructions for the study, (3) or if the sponsor stops the study for administrative or any other reasons."
- Under section **Questions**, line 3 – Please replace the words "**or related concerns**," with the words "**or any related concerns or complaints**,".
- After section **Questions** - Please add a new section titled "**Research Participation Information**" and the following paragraph:

  "You can obtain information about participating in research studies from a number of sources. A few are:
  - Center for Information and Study on Clinical Research Participation (CISCRP): www.ciscrp.org
  - Food and Drug Administration (FDA): www.fda.gov
  - Office for Human Research Protections (OHRP): www.hhs.gov/ohrp
  - National Institute of Health: clinical trials.gov
  - National Cancer Institute: www.nci.nih.gov
  - CenterWatch: www.centerwatch.com
  - Various large university websites
  - Various associations and societies concerned with specific diseases websites."

Page 10:

- Under section **Consent** - Please replace the words "Signature of Witness" with the words "Signature of Person Obtaining Consent". Then reformat to move the "Signature of Person Obtaining Consent" and "Date" line to its own line below the Printed Name of Subject" line.

Please forward the revisions to our office as soon as possible. If any of the revisions can not be made due to the EPA, please just note as such in your cover letter. You may e-mail the revisions to me. If you have any questions, please call.

Thanks.

Karen Radcliffe
908-236-7735 (Office)
908-236-2027 (Fax)
kradcliffe@essexirb.com

Nick Spero

From: "Nick Spero" <nspero@icrlab.com>
To: "Karen Radcliffe" <kradcliffe@essexirb.com>
Sent: Tuesday, February 19, 2008 5:03 PM
Subject: Re: Avon #G0590607001A117

Karen,

I will make the changes and send them tomorrow.

Thanks,
Nick

Nick C. Spero
Associate Director of Operations
ICR, Inc.
1330 Dillon Heights Ave.
Baltimore, MD 21228-1199
Phone (410)747-4500
Fax (410) 747-4928
www.icrlab.com

----- Original Message -----
From: Karen Radcliffe
To: nspero@ICRlab.com
Sent: Tuesday, February 19, 2008 2:37 PM
Subject: Avon #G0590607001A117

Hi Nick:

The **Amended Protocol** (dated 2-8-08), reviewed by a full Board, was **approved on February 18, 2008.**

The **Revised Consent Form** (dated 2-8-08) was **conditionally approved** pending the following modifications:

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- Under section **Benefits**, 2nd paragraph, line 2 – Please replace the words "**a potentially important public health pest.**" with the words "**a noxious pest.**"
- Under section **Alternative** – Please rewrite this sentence as follows: "**The only alternative is not to participate.**"
- After section **Alternative** - Please add a new section titled "**NEW INFORMATION**" and add the following paragraph: "You will be informed verbally or in writing of any significant new findings discovered during the course of this study which may influence your continued participation."
- After the new section **New Information** – Please add a new section titled **Voluntary Participation/Withdrawal** and add the following new paragraph: "You may be withdrawn from the study even if you want to continue. This could happen if (1) the study doctor believes it is in your best interest for you to stop being in the study, (2) or if you do not follow instructions for the study, (3) or if the sponsor stops the study for administrative or any other reasons."
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"You can obtain information about participating in research studies from a number of sources. A few are:

- Center for Information and Study on Clinical Research Participation (CISCRP): www.ciscrp.org
- Food and Drug Administration (FDA): www.fda.gov
- Office for Human Research Protections (OHRP): www.hhs.gov/ohrp
- National Institute of Health: clinical trials.gov
- National Cancer Institute: www.nci.nih.gov
- CenterWatch: www.centerwatch.com
- Various large university websites
- Various associations and societies concerned with specific diseases websites."

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- Under section **Consent** - Please replace the words "Signature of Witness" with the words "Signature of Person Obtaining Consent". Then reformat to move the "Signature of Person Obtaining Consent" and "Date" line to its own line below the Printed Name of Subject" line.

Please forward the revisions to our office as soon as possible. If any of the revisions can not be made due to the EPA, please just note as such in your cover letter. You may e-mail the revisions to me. If you have any questions, please call.

Thanks.

Karen Radcliffe
908-236-7735 (Office)
908-236-2027 (Fax)
kradcliffe@essexirb.com

Nick Spero

From: "Nick Spero" <nspero@icrlab.com>
To: "Karen Radcliffe" <kradcliffe@essexirb.com>
Sent: Wednesday, February 20, 2008 12:53 PM
Attach: ICD w changeswirbchangesaccepted2-20.doc
Subject: Revised ICD

Karen,

I have attached the revised ICD with all requested changes except the following one:

- Under section **Benefits**, 2nd paragraph, line 2 – Please replace the words "**a potentially important public health pest.**" with the words "**a noxious pest.**"

The EPA specifically cites "Public Health Pests" in their guidelines. To eliminate public health pests and replace with a noxious pest would create problems.

I believe there is at least one inch at the bottom of each page between text and the end of the page, so I did not add any "this space intentionally left blank" boxes.

Please let me know if this will create any issues with Essex.

Regards,

Nick

Nick C. Spero
Associate Director of Operations
ICR, Inc.
1330 Dillon Heights Ave.
Baltimore, MD 21228-1199
Phone (410)747-4500
Fax (410) 747-4928
www.icrlab.com

Nick Spero

From: "Nick Spero" <nspero@icrlab.com>
To: "Karen Radcliffe" <kradcliffe@essexirb.com>
Cc: <nspero@icrlab.com>
Sent: Wednesday, February 20, 2008 3:01 PM
Attach: to Karen ICD w changeswirbchangesaccepted2-20.doc
Subject: try this one

Hello Karen,
I made sure the ICD was saved as 97-2003 in Word. Please let us know if you still have problems with the document.

Thanks,
Ellen
Nick C. Spero
Associate Director of Operations
ICR, Inc.
1330 Dillon Heights Ave.
Baltimore, MD 21228-1199
Phone (410)747-4500
Fax (410) 747-4928
www.icrlab.com

Nick Spero

From: "Karen Radcliffe" <kradcliffe@essexirb.com>
To: <nspero@ICRlab.com>
Sent: Tuesday, February 26, 2008 11:18 AM
Attach: G0590607001A117 Consent 2-20-08 Stamped.pdf; Amend. 9 Apprv.Ltr..tif
Subject: Avon #G0590607001A117 Amend. Approval

Hi Nick:

Attached is the Amendment # 9 Approval Letter and approved, stamped Revised Consent for the G0590607001A117 study. The original, hard-copies will be sent to you via FedEx tonight. If you have any questions, please call.

Thanks.

Karen Radcliffe
908-236-7735 (Office)
908-236-2027 (Fax)
kradcliffe@essexirb.com

Nick Spero

From: "Nick Spero" <nspero@icrlab.com>
To: "Karen Radcliffe" <kradcliffe@essexirb.com>
Sent: Tuesday, February 26, 2008 2:12 PM
Subject: Re: Avon #G0590607001A117 Amend. Approval

Karen,

Thanks very much.

Robin for Nick
Nick C. Spero
Associate Director of Operations
ICR, Inc.
1330 Dillon Heights Ave.
Baltimore, MD 21228-1199
Phone (410)747-4500
Fax (410) 747-4928
www.icrlab.com

----- Original Message -----
From: Karen Radcliffe
To: nspero@ICRlab.com
Sent: Tuesday, February 26, 2008 10:18 AM
Subject: Avon #G0590607001A117 Amend. Approval

Hi Nick:

Attached is the Amendment # 9 Approval Letter and approved, stamped Revised Consent for the G0590607001A117 study. The original, hard-copies will be sent to you via FedEx tonight. If you have any questions, please call.

Thanks.

Karen Radcliffe
908-236-7735 (Office)
908-236-2027 (Fax)
kradcliffe@essexirb.com

Nick Spero

From: "Karen Radcliffe" <kradcliffe@essexirb.com>
To: <nspero@ICRlab.com>
Sent: Thursday, March 06, 2008 12:32 PM
Attach: G0590607001A117 Stamped Protocol.tif; G0590607001A117 General Meeting Minutes 2-18-08.tif
Subject: Avon #G0590607001A117

Hi Nick:

I apologize for not sending this to you yesterday. Attached is the approved, stamped Protocol cover page for the Avon study. Also attached is the General Minutes with your Amendment listed. I will send out the originals to you in tonight's FedEx. If you have any questions, please call.

Thanks.

Karen Radcliffe
908-236-7735 (Office)
908-236-2027 (Fax)
kradcliffe@essexirb.com

Nick Spero

From: "Nick Spero" <nspero@icrlab.com>
To: "Karen Radcliffe" <kradcliffe@essexirb.com>
Sent: Thursday, March 06, 2008 1:20 PM
Subject: Re: Avon #G0590607001A117

Karen,

Thank you for your help.

Regards,
Nick

Nick C. Spero
Associate Director of Operations
ICR, Inc.
1330 Dillon Heights Ave.
Baltimore, MD 21228-1199
Phone (410)747-4500
Fax (410) 747-4928
www.icrlab.com

> ----- Original Message -----
> **From:** Karen Radcliffe
> **To:** nspero@ICRlab.com
> **Sent:** Thursday, March 06, 2008 11:32 AM
> **Subject:** Avon #G0590607001A117
>
> Hi Nick:
>
> I apologize for not sending this to you yesterday. Attached is the approved, stamped Protocol cover page for the Avon study. Also attached is the General Minutes with your Amendment listed. I will send out the originals to you in tonight's FedEx. If you have any questions, please call.
>
> Thanks.
>
> **Karen Radcliffe**
> 908-236-7735 (Office)
> 908-236-2027 (Fax)
> kradcliffe@essexirb.com

ICR | *Independent Laboratory*
Pesticide Efficacy Testing
Regulatory Services

March 14, 2008

Chairman
Essex Institutional Review Board, Inc.
121 Main Street
Lebanon, NJ 08833-2162

Protocol # G0590607001A117 **ICR Project # 0607-059-0157**
Version Date February 8, 2008

Dear Dr. Lambert:

Please find enclosed a deviation page for the following protocol :

Protocol # G0590607001A117 ICR Project # 0607-059-0157
Version Date February 8, 2008.

This deviation did not impact the study or the test subjects.

Please acknowledge receipt of this deviation via email.

Thank you for your attention, and please do not hesitate to contact me by telephone at 410-747-4500, by fax at 410-747-4928, or email address nspero@icrlab.com if you have any questions.

Sincerely,

Niketas C. Spero
Principal Investigator

Enclosures

1330 Dillon Heights Avenue, Baltimore, MD 21228-1199 | **tel** 410.747.4500 | **fax** 410.747.4928 | **web** www.icrlab.com

ICR, INC
1330 Dillon Heights Avenue
Baltimore, MD 21228
Telephone: (410) 747-4500
Fax: (410) 747-4928

Protocol Deviation

Project Number:	0607-059-0157
Protocol Number:	G0590607001A117
Sponsor:	Avon Products, Incorporated
Test Article(s):	TA# 1001108-030
	TA# 1004024-010
GLP Compliance:	40 CFR 160
Deviation:	The protocol states that subjects will be treated in pairs and the treatment time will be when the application of the second test article begins. However, six subjects were treated sequentially and the treatment time was recorded when the application of the second test article began. This was done to minimize confusion among treated subjects regarding when they were required to enter the insectary for the next half hourly exposure to mosquitoes.
Impact On The Study:	There is no impact on the study.

Submitted by: _____ 3-13-08 Date

Acknowledged by QA: _____ 3/13/08 Date

Acknowledged by: Sponsor Representative _____ 3/6/08 Date

ICR | Independent Laboratory Pesticide Efficacy Testing Regulatory Services

RECEIVED
MAR 17 2008
Essex Institutional Review Board, Inc.

March 14, 2008

Chairman
Essex Institutional Review Board, Inc.
121 Main Street
Lebanon, NJ 08833-2162

Protocol # G0590607001A117 **ICR Project # 0607-059-0157**
Version Date February 8, 2008

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Please find enclosed a deviation page for the following protocol :

Protocol # G0590607001A117 ICR Project # 0607-059-0157
Version Date February 8, 2008.

This deviation did not impact the study or the test subjects.

Please acknowledge receipt of this deviation via email.

Thank you for your attention, and please do not hesitate to contact me by telephone at 410-747-4500, by fax at 410-747-4928, or email address nspero@icrlab.com if you have any questions.

Sincerely,

Niketas C. Spero
Principal Investigator

Enclosures

RECEIVED
MAR 17 2008
KB

1330 Dillon Heights Avenue, Baltimore, MD 21228-1199 | tel 410.747.4500 | fax 410.747.4928 | web www.icrlab.com

ICR, INC
1330 Dillon Heights Avenue
Baltimore, MD 21228
Telephone: (410) 747-4500
Fax: (410) 747-4928

Protocol Deviation

Project Number: 0607-059-0157

Protocol Number: G0590607001A117

Sponsor: Avon Products, Incorporated

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TA# 1004024-010

GLP Compliance: 40 CFR 160

Deviation: The protocol states that subjects will be treated in pairs and the treatment time will be when the application of the second test article begins. However, six subjects were treated sequentially and the treatment time was recorded when the application of the second test article began. This was done to minimize confusion among treated subjects regarding when they were required to enter the insectary for the next half hourly exposure to mosquitoes.

Impact On The Study: There is no impact on the study.

Submitted by: [signature] 3-13-08 Date

Acknowledged by QA: [signature] 3/13/08 Date

Acknowledged by: Sponsor Representative [signature] 3/6/08 Date

Essex Institutional Review Board, Inc.
121 Main Street • Lebanon, New Jersey 08833
Telephone (908) 236-7735 • Fax (908) 236-2027
www.essexirb.com

February 19, 2008

On **February 18, 2008**, the Board met at 121 Main Street, Lebanon, NJ 08833 at 4:00 p.m. Board members present: **Glenn P. Lambert, MD** (Chairman) **Nancy Maulding** and **Thomas G. McElrath, MD**. Alternate Board Members: **John Castro** (Alternate for Philip B. Carr-Jones) and **Harry M. Woske, MD** (Alternate for Loretta P. Szczepanski, RN). The following individuals were also present to take minutes: Karen Radcliffe Glenn P. Lambert, MD, FAAP chaired the meeting.

Glenn P. Lambert, MD called the meeting to order at 4:00 p.m.

Old Business
Investigator 483 Reports received during the previous week were made available for Board review and discussion. Observations of the FDA inspection and the response of the principal investigator were assessed. The Board recommended approval of the investigator(s) to continue to conduct the study [or to be eligible to conduct future studies].

Other agenda items: periodic reviews/extension requests, increased enrollment requests, final reports, **amendments** (no risk changes), expedited reviews, periodic protocol reviews, study site approvals, site closures, complaints from participants, consideration of local ethical standards, and safety reports were presented with the recommendations by the Chairman. There being no further questions, approvals were granted in accordance with the Chairman's recommendations.

Glenn P. Lambert, MD reported to the Board the following **Expedited Reviews** for the week ending on **February 18, 2008:**

- **Other Study Sponsors & Number Omitted**

The following studies were granted **Periodic Protocol Review** approval by the Board on **February 18, 2008**:

- **Other Study Sponsors & Number Omitted**

The following **Protocol Amendments** were granted approval by the Board on **February 18, 2008**:

- **Avon Products, Inc. (G0590607001A117)**
- **Other Study Sponsors & Number Omitted**

Glenn P. Lambert, MD reported to the Board the following **Site Approvals** for the week ending on **February 18, 2008:**

- **Other Study Sponsors & Number Omitted**

The following **Conflict of Interest Statements** made by the following Investigators were granted approval by the Board on **February 18, 2008**:

- **Other Investigators, Study Sponsors & Number Omitted**

New Business

NO NEW BUSINESS THIS WEEK

Motion was called to approve or conditionally approve the studies. There being no further discussion the roll was called. Motion carried. All meeting votes were unanimous with a vote of 5:0 with a sustained quorum.

There were no controverted issues and there was no conflict of interest for any of the Board members in attendance. Approvals will be for one year from date of site notification.

The meeting adjourned at **5:20 pm.**

Karen Radcliffe — 2-19-08
Karen Radcliffe — 2-19-08

G. L. Lambert — 2-19-08

eirb

Essex Institutional Review Board, Inc.
121 Main Street • Lebanon, New Jersey 08833
Telephone (908) 236-7735 • Fax (908) 236-2027
www.essexirb.com

MEMBERS

Philip B. Carr-Jones, M Div
Episcopal Priest

Loretta P. Szczepanski, RN
EIRB Vice-Chairperson
Registered Nurse

Glenn P. Lambert, MD, FAAP
EIRB Chairman
Pediatrician

Tom Ollis, R Ph
EIRB Vice-Chairman
Pharmacist

Thomas G. McElrath, MD
Obstetrician/Gynecologist

Deborah A. Timmerman
Office Administrator

Nancy Maulding
Mathematician

ALTERNATE MEMBERS

John Castro
Engineer/Airline Pilot

Sandra S. Sullivan, OTR
Occupational Therapist

Louise M. Dougherty, RN
Registered Nurse

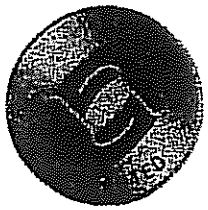
Jorshinelle T. Sonza, PhD
Playwright/Writer

Vassie C. Ware, PhD
Molecular Biologist

Harry M. Woske, MD
Cardiologist

James L. Harris
Chemist/Business Manager

eirb
Essex Institutional Review Board, Inc.
121 Main Street • Lebanon, New Jersey 08833
Telephone (908) 236-7735 • Fax (908) 236-2027
www.essexirb.com



Ellen Quinn
Associate Director, Administration
Insect Control & Research, Inc.
1330 Dillon Heights Avenue
Baltimore, MD 21228

Re: Essex IRB Members

Dear Ellen:

Per your request for the profiles of the members of the Essex IRB, I enclose the following information:

Members:

Glenn P. Lambert, MD, FAAP: BS; Chairman; Board-Certified in Pediatrics, 29 years of IRB experience, full-time employee for 7 years

Loretta P. Szczepanski, RN; Vice-Chairperson; BSN, MA/Administration, CNA, Registered Nurse; retired Director of Patient Care Services Hunterdon Medical Center; 5 years on Board

Philip B. Carr-Jones, BA, M Div; Episcopal Priest; 14 years on Board

Deborah A. Timmerman: HS degree; homemaker, bookkeeper/secretary/office manager; 13 years on Board

Tom Ollis, R Ph; BS, MA of Administrative Science; hospital pharmacist; 5 years on Board

Thomas G. McElrath, MD, FACOG; Ob/Gyn specialist; 3 years on Board

Nancy Maulding, BS, MAT; Professor of Mathematics; 2 years on Board

Alternate Members:

Louise M. Dougherty, RN, BSN, MS in Education; Public Health Nurse; 5 years on Board

~~John Castro, BS Engineering; Airline Pilot; 2 years on Board~~

Sandra S. Sullivan, OTR, BS; Occupational Therapist; 2 years on Baord

Jorshinelle T. Sonza, PhD; Playwright and author; BA, MA, PhD in English and Comparative Literature; 4 years on Board

Vassie C. Ware, PhD, BA, MPhil; Professor of Molecular Biology, Lehigh University; 6 years on Board

Harry M. Woske, MD; FACC, FACP; AB; Cardiologist; 5 years on Board

James L. Harris, BS, MBA; Chemist/Business Manager; 1 year on Board

William C. Waggoner, PhD, FAACT, AB, MS; Toxicologist, medical ethicist, CEO/President of Essex IRB; Board chairman from 1981 to 1999; on Board as an ex officio member for 3 years

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Thank you for using Essex IRB for your studies.

Sincerely,

Glenn P. Lambert, MD

Glenn P. Lambert, MD, FAAP
Chairman

ICR | *Independent Laboratory*
Pesticide Efficacy Testing
Regulatory Services

March 18, 2007

Subject: Follow-up call to test subjects from the following repellent study:

PROTOCOL NUMBER: G0590607001A117
PROJECT NUMBER: 0607-059-0157
STUDY TITLE
EVALUATION OF THE EFFICACY OF PERSONAL REPELLENTS AGAINST MOSQUITOES IN THE LABORATORY

All test subjects were contacted within two weeks of the conduct of the study to see I they experienced any adverse effects related to this study. None of the test subjects indicated that they had any adverse effects from participating in the study.

Niketas C. Spero
Study Director

1330 Dillon Heights Avenue, Baltimore, MD 21228-1199 | tel 410.747.4500 | fax 410.747.4928 | web www.icrlab.com

Journal of the American Mosquito Control Association, 15(3):348–355, 1999

VARIATION IN THE PROTECTION PERIODS OF REPELLENTS ON INDIVIDUAL HUMAN SUBJECTS: AN ANALYTICAL REVIEW[1]

L. C. RUTLEDGE[2] AND R. K. GUPTA[3]

ABSTRACT. Mosquito repellent test data from the literature were analyzed to estimate mean protection periods and among-subjects standard deviations. Standard deviations were a linear function of the means. Numbers of subjects needed to determine mean protection periods of 1–8 h with confidence limits of ±0.5, 1.0, 1.5, and 2.0 h at the 99 and 95% levels of confidence were computed from regression values of the standard deviation, and a table of sample sizes was constructed for use in planning repellent tests.

KEY WORDS Repellents, insect repellents, mosquito repellents

INTRODUCTION

Wadley (1946) reported that 5 subjects differed significantly in periods of protection obtained from 6 repellents in tests against *Aedes aegypti* (L.). The among-subjects standard deviation was 2.0 h. However, review of the literature shows that the among-subjects standard deviation differs among studies. This is to be expected, because sample standard deviations are themselves variable, with the standard error of a sample standard deviation from a normal population being $\sigma/\sqrt{(2n)}$.

Because the size of sample needed to estimate the mean of a normal population with a specified degree of precision at a specified level of confidence is determined by the standard deviation, it is desirable to estimate the among-subjects standard deviation of protection periods as accurately as possible for efficient planning of repellent tests.

The present study analyzed data from previous studies to estimate mean protection periods and among-subjects standard deviations. The estimates so obtained were further analyzed to estimate the numbers of subjects needed for selected degrees of precision and levels of confidence in the determination of protection periods.

MATERIALS AND METHODS

Computation of means and standard deviations: Twenty-two estimates of mean and standard deviation were obtained from 19 source studies (Table 1). Relevant parameters of the data analyzed are given in Table 2. Because the data reported and the experimental designs employed in the source studies were variable, methods of computation employed in the study will be described here in general terms only. Specifics of the methods employed are documented in the Appendix.

Walker and Lev (1953) provided formulas for computing the mean of a total group, sum of squares among groups, and sums of squares within groups, when only group means, number of cases, and variance or standard deviation are given. Fisher and Yates (1963) provided formulas and tables for estimating the standard deviation from the range and sample size. Langley (1970) provided formulas for combining means or standard deviations of random samples of the same statistical population. Mandel (1984) provided formulas for pooling the means of samples having different standard deviations or the standard deviations of samples having different means. In most cases, these formulas and tables were sufficient for purposes of the study.

Protection period is defined as the period between the time of application of the repellent and the time of occurrence of a specified end point, commonly the 1st or 2nd observed bite. If the test is terminated before the end point is reached, the result is reported as an inequality (e.g., >120 or "120+" min). Although the standard deviation can not be computed from data containing inequalities (Rutledge 1988), deletion of the inequalities introduces bias, because the values deleted are larger than those retained. Therefore, in the present study, repellents for which inequalities were reported were excluded from analysis. Repellents having long protection periods may be correspondingly underrepresented.

Because each source study was unique and may or may not have common factors with any other, mean protection periods were computed as the means of the observed protection periods, without adjustment for specific factors or variables operating in the source study. Protection periods and standard deviations reported in minutes were converted to hours for comparative purposes.

To simplify computations, among-subjects standard deviations were computed without adjustment for correlation of means and standard deviations within source studies. This approximation exaggerates the estimate of among-subjects standard deviation, although variation within studies is usually smaller than variation among studies. The bias is

[1] Opinions and assertions herein should not be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. Use of trade names does not imply official endorsement or approval of the products named.

[2] 11 Circle Way, Mill Valley, CA 94941–3420.

[3] U.S. Army Medical Research & Materiel Command, ATTN: MCMR-MSI, 504 Scott Street, Fort Detrick, MD 21702–5012.

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Table 1. Sources of the data analyzed.

Reference no.[1]	Citation	Data analyzed
1	Gilbert et al. (1966)	Table 1, men
2	Gilbert et al. (1966)	Table 1, women
3	Traub and Elisberg (1962)	Table 3, repellent M-2020
4	Altman (1969)	Tables 1–3
5	Applewhite and Smith (1950)	Tables 1 and 2
6	Dua et al. (1996)	Page 407
7	Gouck and Bowman (1959)	Table 3
8	Smith et al. (1963)	Tables 5–9, 11, 12, 15, 19
9	Pijoan et al. (1946)	Table 1
10	Schreck and Smith (1977)	Table 2, Series 1
11	Travis (1950)	Table 1
12	Whittemore et al. (1961)	Table 2
13	Traub and Elisberg (1962)	Table 3, deet
14	Wadley (1946)	Page 31
15	Spencer et al. (1977)	Table 1
16	Wiesmann and Lotmar (1949)	Table 1
17	Spencer et al. (1976)	Table 3
18	Wiesmann and Lotmar (1949)	Page 299
19	Spencer and Akers (1976)	Table 1
20	Rietschel and Spencer (1975)	Table
21	Skinner et al. (1977)	Table 1
22	Reifenrath and Akers (1981)	Table 2

[1] Identifies corresponding entries in Tables 2 and 3 and the Appendix.

conservative in the sense that it maximizes the estimate of the among-subjects standard deviation and leads to a larger estimate of the number of subjects required.

The number of subjects employed in certain source studies was unclear because of uncertainty as to whether the same or different subjects were employed in tests conducted at different times and places. In such cases, the number of subjects was taken to be the minimum number needed to account for the data analyzed. This approach is conservative in the sense that it maximizes the estimate of the among-subjects standard deviation.

Where the source study reported observed or

Table 2. Relevant parameters of the data analyzed.

Reference no.[1]	State or country	Setting	Mosquito species	Test materials	Test subjects
1	Florida	Laboratory	1	1	50
2	Florida	Laboratory	1	1	50
3	Malaysia	Field	3	1	10
4	Panama	Field	1	2	5
5	Alaska	Field	4	13	9
6	India	Laboratory	1	1	5
7	Florida	Laboratory	1	3	3
8	Florida	Laboratory	1	3	8
9	Maryland	Laboratory	1	2	3
10	Florida	Field	1	2	5
11	Florida	Laboratory and field	4	12	6
12	Texas	Field	1	2	10
13	Malaysia	Field	3	1	10
14	Florida	Laboratory	1	6	5
15	California	Laboratory	1	4	8
16	Argentina	Field	8	2	8
17	California	Laboratory	1	7	16
18	France	Field	2	1	6
19	Florida	Field	1	3	4
20	California	Laboratory	1	1	16
21	California	Laboratory	1	1	11
22	California	Field	1	2	4

[1] See corresponding entry in Table 1 for identification of source study.

Table 3. Mean protection periods and standard deviations.

Reference no.[1]	Mean (h)	Standard deviation (h)
1	0.48	0.65
2	0.65	0.52
3	1.06	0.21
4	1.06	0.59
5	1.38	0.94
6	1.90	0.40
7	2.14	2.97
8	2.20	3.09
9	2.71	0.51
10	3.23	0.58
11	3.32	4.08
12	3.41	0.44
13	3.98	1.71
14	4.44	1.99
15	4.75	2.54
16	5.50	2.77
17	5.70	2.55
18	5.72	0.85
19	6.37	1.84
20	6.45	1.69
21	6.93	4.41
22	8.50	4.40

[1] See corresponding entry in Table 1 for identification of source study.

mean protection periods obtained on individual subjects, the among-subjects mean square was computed by analysis of variance, and the standard deviation was obtained as the square root of the among-subjects mean square. One-way, 2-way, or other conventional statistical designs were employed where possible.

Multivariate methods were employed to analyze data compiled from disparate experiments on the same subjects and to analyze data from experiments with asymetrical structure and/or missing or excluded observations. Because order of effects is important in multivariate statistical analyses (Mead 1990), effects attributable to subjects were given priority over other factors. This approach is conservative in the sense that it maximizes the estimate of the among-subjects standard deviation.

Where the source study reported among-subjects ranges and/or standard deviations of protection periods separately for 2 or more tests, the combined standard deviation was computed as described by Mandel (1984) from pooled sums of squares obtained by back-calculation from the among-subjects ranges or standard deviations (Fisher and Yates 1963, Mandel 1984).

Analysis of means and standard deviations: A linear regression of standard deviations on mean protection periods was computed. In computing the regression, observations were weighted by the number of subjects tested, as shown in Table 2. Means, standard deviations, and residuals from regression were tested for outlying observations by Grubb's test (Dunn and Clark 1974).

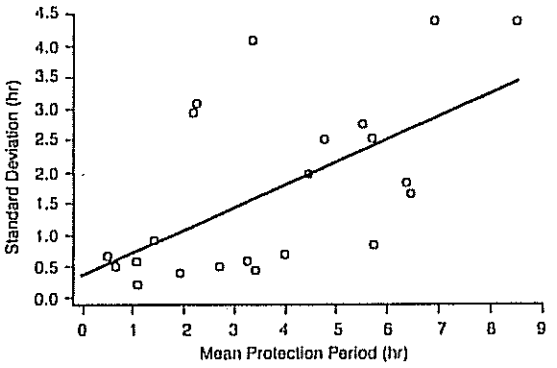

Fig. 1. Linear regression of standard deviations on mean protection periods: $Y = 0.3705 + 0.3596X$.

Sampling table: A table was constructed to provide numbers of subjects needed to determine protection periods of 1–8 h with confidence limits of ±0.5, 1.0, 1.5, and 2.0 h at the 99 and 95% levels of confidence. Estimates of required sample sizes were computed from the standard deviation as described by Martin and Bateson (1993).

RESULTS AND DISCUSSION

Means and standard deviations

Mean protection periods computed from the data identified in Table 1 ranged from 0.48 h (data of Gilbert et al. 1966) to 8.50 h (data of Reifenrath and Akers 1981) (Table 3). The extreme values were not significant by Grubb's test for outliers ($T_1 = 1.419$, $T_{22} = 2.092$, $n = 22$, $P > 0.05$).

Standard deviations computed from the data identified in Table 1 ranged from 0.21 h (data of Traub and Elisberg 1962) to 4.41 h (data of Skinner et al. 1977) (Table 3). The extreme values were not significant by Grubb's test for outliers ($T_1 = 1.114$, $T_{22} = 1.905$, $n = 22$, $P > 0.05$).

Analysis

The linear regression of standard deviations on mean protection periods was

$$Y = 0.3705 + 0.3596X,$$

where Y is the standard deviation and X is the mean protection period (Fig. 1). The residuals from regression ranged from −1.58 h (data of Wiesmann and Lotmar 1949) to +2.52 h (data of Travis 1950). The extreme values were not significant by Grubb's test for outliers ($T_1 = 1.461$, $T_{22} = 2.209$, $n = 22$, $P > 0.05$).

The coefficient of correlation was significant ($r = 0.60$, df = 20, $P < 0.05$). The coefficient of determination ($r^2 = 0.51$) indicated that 51% of the observed variation in the standard deviations was

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Protection period (h)	Standard deviation[1] (h)
1	0.73
2	1.09
3	1.45
4	1.81
5	2.17
6	2.53
7	2.89
8	3.25
1	0.73
2	1.09
3	1.45
4	1.81
5	2.17
6	2.53
7	2.89
8	3.25

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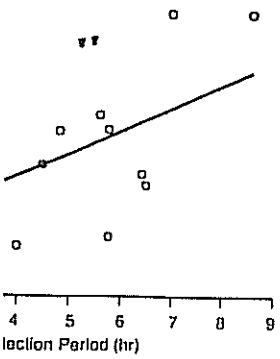

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DISCUSSION

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attributable to variation in mean protection periods. The remaining variation can be attributed to variation in species, climate, season, weather, materials and methods, and other variables associated with the respective source studies (Table 2).

Note added in revision: At the suggestion of an anonymous reviewer (Reviewer 1), additional analyses were performed to determine if the effects of locale (state/country) or setting (laboratory/field) (Table 2) on protection periods were significant. Neither factor was significant when included in the analysis ($F = 0.65$, df = 9,9, $P > 0.05$ and $F = 3.13$, df = 2,9, $P > 0.05$, respectively).

The original version of this paper included chi-square tests for goodness of fit of the observed distributions of means, standard deviations and residuals to the normal distribution (Steel and Torrie 1980). Values of χ^2 were not statistically significant ($\chi^2 = 0.95$, df = 3, $P > 0.05$ for means; $\chi^2 = 7.15$, df = 3, $P > 0.05$ for standard deviations; $\chi^2 = 4.65$, df = 3, $P > 0.05$ for residuals).

However, Reviewer 1 found that the distribution of standard deviations differed significantly from normal in a computer simulation and by the Kolmogorov–Smirnov test, the Box–Cox procedure, and the plot of order statistics. On the basis of the Box–Cox analysis, Reviewer 1 reanalyzed the data using a logarithmic transformation of the standard deviations, concluding that "the sample sizes [so obtained] were not too different [from those of Table 4], so that the extra effort was not overly fruitful and the interpretation of the simpler model was lost."

Similarly, an in-house reviewer (Reviewer 3) found that the distribution of standard deviations differed significantly from normal by the Anderson–Darling test. On this basis, Reviewer 3 fitted a quadratic (2nd degree polynomial) curve to the data, concluding that "the fitted values for standard deviation based on quadratic fit to the smoothed data show[ed] little difference [from those based on linear regression] through 7 h [of protection]."

In an additional analysis, Reviewer 3 grouped source studies with similar mean protection periods to compute the bias error, pure error, and F value for lack of fit (Draper and Smith 1981). Because the value of F was not statistically significant, Reviewer 3 concluded that the F test for lack of fit provided no reason to doubt the adequacy of the linear regression model.

According to Draper and Smith (1981), the ratio of the F value for regression to the tabulated value must be ≥4 for the regression to be useful, as opposed to being merely significant. Reviewer 3 found that this ratio was 4.75 in the present study and concluded that the regression model was useful. In this connection, Martin and Bateson (1993) have suggested that the correlation observed in the study ($r = 0.60$) can be interpreted as moderate,

Table 4. Numbers of subjects needed to determine protection periods of 1–8 h with confidence limits of ±0.5–2.0 h at the 99 and 95% levels of confidence.[1]

Protection period (h)	Standard deviation[2] (h)	D = 0.5 h	D = 1.0 h	D = 1.5 h	D = 2.0 h
		$\alpha = 0.01$			
1	0.73	15	4	2	1
2	1.09	32	8	4	2
3	1.45	56	14	7	4
4	1.81	87	22	10	6
5	2.17	125	32	14	8
6	2.53	170	43	19	11
7	2.89	222	56	25	14
8	3.25	280	70	32	18
		$\alpha = 0.05$			
1	0.73	9	3	1	1
2	1.09	19	5	3	2
3	1.45	33	9	4	3
4	1.81	51	13	6	4
5	2.17	73	19	9	5
6	2.53	99	25	11	7
7	2.89	129	33	15	9
8	3.25	163	41	19	11

[1] Numbers of subjects were computed from the formula: $n = (s^2 z_{\alpha/2}^2)/D^2$, where n is the number of subjects, s is the standard deviation, $z_{\alpha/2}$ is the critical value of the cumulative normal variable z at the $\alpha/2$ level of significance, α is the level of statistical significance to be attached to the estimate, and D is the maximum acceptable difference between the sample mean and the true (population) mean (Martin and Bateson 1993). Results of computation were rounded to the next higher integer, as the number of subjects cannot be fractional.

[2] Standard deviations were computed from the regression equation $Y = 0.3705 + 0.3596X$, where Y is the standard deviation and X is the mean protection period (see text).

indicating a substantial relationship of means and standard deviations.

In a further analysis, Reviewer 3 identified observations 1 and 2 as particularly influential and reanalyzed the data with those observations deleted to determine their effect on the conclusions of the study. Reviewer 3 concluded that "The prediction equation was hardly altered by deleting these two observations, but the . . . ratio of F values fell . . . to 1.9." Because neither the X values (0.48 and 0.65, respectively) nor the Y values (0.65 and 0.52, respectively) of observations 1 and 2 were significant outliers (see above), we suggest that the relatively large influence of observations 1 and 2 reflects the relatively large weights assigned to those observations in the regression analysis (Table 2).

Our decision to retain the original (linear regression) analysis was based on several considerations. In our opinion, a point exists beyond which increasingly refined and sophisticated statistical analyses yield diminishing returns in terms of clarity and credibility of presentation. Many phenomena result in data distributed in a manner sufficiently normal to provide the basis of theory in biology and other fields of application (Steel and Torrie 1980). In the present case, neither logarithmic transformation (Reviewer 1) nor quadratic curve fitting (Reviewer 3) materially changed the outcome of the analysis. Testing for lack of fit, useful regression, and influential observations (Reviewer 3) tended to support the linear regression model.

Sampling table

Because the among-subjects standard deviation of protection periods is a function of the mean, it is necessary to know an approximate value of the mean to compute the number of subjects needed to determine the mean precisely. This requirement for advance knowledge of the parameter to be estimated is common in repellent studies (Rutledge et al. 1989) and in bioassay studies in general (Finney 1978).

Table 4 provides estimated among-subjects standard deviations for mean protection periods of 1–8 h and the corresponding numbers of subjects needed to determine the mean protection period with confidence limits of ±0.5, 1.0, 1.5, and 2.0 h at the 99 and 95% levels of confidence. Given the uncertainty in the standard deviations from which the sample sizes were derived, the values shown should be regarded as guidelines only. However, uncertainties in the source studies were interpreted conservatively (see the Materials and Methods section and the Appendix), and we believe that the values given will be found useful in practice.

This paper is the 1st published attempt to determine the number of subjects needed in repellent tests. Additional research is needed to refine and extend Table 4, taking into account variation in species, climate, season, weather, materials and methods, and other variables present in repellent tests.

ACKNOWLEDGMENTS

We thank an anonymous reviewer of the *Journal of the American Mosquito Control Association* (Reviewer 1) and J. R. Burge of the Walter Reed Army Institute of Research (Reviewer 3) for their incisive and thorough reviews of the manuscript.

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VLEDGMENTS

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APPENDIX

This Appendix documents the methods used in computing the means and standard deviations shown in Table 3 from the data identified in Table 1. The information provided is not essential for understanding the body of the report. Section numbers of the Appendix correspond with the reference numbers of Tables 1–3. Symbols and terms follow Steel and Torrie (1980). The terms "mean square" and "variance" are equivalent.

Methods of computing means from data that do not include the observed values were described by Walker and Lev (1953) and Langley (1970) and will not be repeated here. For brevity, the methods described for computing among-subjects standard deviations are considered complete when the variance attributable to subjects is obtained, with further computation of the standard deviation as the square root of the variance being understood.

Where source studies reported among-subjects ranges and/or standard deviations of protection periods separately for 2 or more tests, the combined standard deviation was computed as described by Mandel (1984) from pooled sums of squares obtained by back-calculation from the among-subjects ranges or standard deviations (Fisher and Yates 1963, Mandel 1984). For brevity, this procedure is referred to as "pooling."

1) Gilbert et al. (1966, Table 1, men) reported the among-subjects range of means of 4 "readings" of the protection period of deet on 50 men in tests against *Ae. aegypti*. The standard deviation corresponding to the stated range was obtained from Table XX of Fisher and Yates (1963) and multiplied by $\sqrt{4}$ to obtain the among-subjects standard deviation on a per-observation basis (Steel and Torrie 1980:142).

2) Gilbert et al. (1966, Table 1, women) reported the among-subjects range of means of 4 "readings" of the protection period of deet on 50 women in tests against *Ae. aegypti*. The among-subjects standard deviation was obtained as described in Section 1.

3) Traub and Elisberg (1962, Table 3, repellent M-2020) reported among-subjects standard deviations obtained in 6 determinations of the protection period of repellent M-2020 on 10 subjects in tests against a natural association of mosquitoes in Malaysia. The 6 standard deviations were pooled to obtain the combined among-subjects standard deviation.

4) Altman (1969, Tables 1–3) reported the observed protection periods of various concentrations of 6 repellents on 5 subjects in tests against *Anopheles albimanus* Wiedemann in Panama. The present analysis was limited to 50% *N,N*-diethylbenzenesulfonamide (Table 1: 2 subjects, 1 replication) and 25% dimethyl phthalate (Table 3: 4 subjects, 2 replications), because certain tests of the other repellents were terminated before completion.

The among-subjects mean square was estimated by multivariate statistical analysis. The model employed in the analysis included the response variable, PROTECTION PERIOD (quantitative), and 2 explanatory variables, SUBJECT (qualitative) and REPELLENT (qualitative). SUBJECT included 5 classes: subjects PB, RA, VA, VB, and WL. REPELLENT included 2 classes: 50% *N,N*-diethylbenzenesulfonamide and 25% dimethyl phthalate.

5) Applewhite and Smith (1950, Tables 1 and 2) determined the protection periods of 10 repellents on 9 subjects in tests against natural associations of mosquitoes at Anchorage (June 29–July3, 1948) and Big Delta (July 8–12), Alaska. Six of the 10 repellents were retested on 5 subjects at Big Delta (July 16–18), and one of the 6 was retested in comparison with 3 additional repellents on 3 subjects at Big Delta and Eilsen Field (July 16–18). In each case, each repellent was tested once on each subject, and the among-subjects range of protection periods was reported.

For purposes of analysis, it was assumed that 9 subjects were employed in the tests and that groups of 3 and 5 subjects were chosen at random from the 9 for the July 16–18 tests. Data from tests of 3 repellents at Anchorage were excluded from analysis, because certain tests of those repellents at that location were terminated before completion. Standard deviations corresponding to the remaining among-subjects ranges were obtained from Table XX of Fisher and Yates (1963) and pooled to obtain the combined among-subjects standard deviation.

6) Dua et al. (1996:407) reported the among-subjects standard deviation of protection periods of an extract of flowers of *Lantana camara* (Verbenaceae) on 5 subjects in tests against *Aedes albopictus* (Skuse). No additional analysis was needed in this case.

7) Gouck and Bowman (1959, Table 3) reported subject means obtained in 4 determinations of the protection periods of 3 repellents on 3 subjects in tests against *Ae. aegypti*. Subject means were converted to totals, and the among-subjects mean square was obtained as in the analysis of variance.

8) Smith et al. (1963, Tables 5–9, 11, 12, 15, 19) reported mean protection periods of varying doses of 3 repellents on 8 subjects in tests against *Ae. aegypti* under varying experimental conditions.

The among-subjects mean square was estimated by multivariate statistical analysis. The model employed in the analysis included the response variable, PROTECTION PERIOD (quantitative), and 5 explanatory variables, DOSE (quantitative), SUBJECT (qualitative), REPELLENT (qualitative), END POINT (qualitative), and SKIN TREATMENT (qualitative). SUBJECT included 8 classes: subjects A–H. REPELLENT included 3 classes: dimethyl phthalate, ethyl hexanediol, and deet. END POINT included 2 classes: the 1st bite and the 5th bite. SKIN TREATMENT included 4 classes: sweated (Table 5), disinfected (Table 6), shaved (Table 15), and normal.

In the source study, doses were reported in terms of concentration (%) and volume (ml) of material applied per forearm (Table 5), weight (g) of material applied per forearm (Table 6), or weight (mg) of material applied per unit area ($in.^2$) of forearm (Tables 7–9, 11, 12, 15, 19). In the present study, doses were converted to mg/cm^2 using appropriate conversion factors and the surface areas of the forearms of the subjects as given in Table 1 of Smith et al. (1963). Because protection periods are proportional to the logarithm of the dose applied (Rutledge et al. 1989), values of DOSE were entered as log mg/cm^2.

Means reported in the source study were based on 1 (Tables 6, 7, 9, 12), 2 (Table 15), 4 (Tables 5, 11, 19), or 6 (Table 8) repetitions of the test procedure. In the present analysis, entries were weighted by the number of repetitions to obtain the among-subjects mean square on a per-observation basis.

9) Pijoan et al. (1946, Table 1) reported the observed protection periods of 2 repellents on 3 subjects in tests against *Ae. aegypti*. Tests were conducted in 4 blocks defined by ambient temperature and humidity and level of physical activity of the subjects. Protection periods were recorded separately for the left and right forearms. In the present study, the data were analyzed as a 2 × 3 × 4 (2 treatments × 3 subjects × 4 blocks) experimental design with duplicate observations (left and right arms) to obtain the among-subjects mean square.

10) Schreck and Smith (1977, Table 2, Series 1) reported among-subjects ranges of the protection periods of 2 repellents on 5 subjects in tests against *Aedes taeniorhynchus* (Wiedemann) in Florida. Standard deviations corresponding to the ranges were obtained from Table XX of Fisher and Yates (1963) and pooled to obtain the combined among-subjects standard deviation.

Note: Ranges reported by Schreck and Smith (1977) in Series 2 and 3 of Table 2 include 2 observations on each subject. Because the ranges refer to observations, not subjects, they could not be used in the study.

11) Travis (1950, Table 1) reported mean protection periods of dimethyl phthalate, butopyronoxyl, and a set of 10 unspecified repellents on 3 (dimethyl phthalate), 6 (butopyronoxyl), or 4 (10 repellents) of 6 subjects in tests against *Anopheles quadrimaculatus* Say (dimethyl phthalate), *Ae. aegypti* (dimethyl phthalate), *Aedes sollicitans* (Walker) (butopyronoxyl), or *Ae. taeniorhynchus* (10 repellents).

The among-subjects mean square was estimated by multivariate statistical analysis. The model employed in the analysis included the response variable, PROTECTION PERIOD (quantitative), and 3 explanatory variables, SUBJECT (qualitative), REPELLENT (qualitative), and SPECIES (qualitative). SUBJECT included 6 classes: subjects 1–6. REPELLENT included 3 classes: dimethyl phthalate, butopyronoxyl, and 10 repellents. SPECIES included 4 classes: *An. quadrimaculatus, Ae. aegypti, Ae. sollicitans,* and *Ae. taeniorhynchus.*

Means reported in the source study were based on 28 (*An. quadrimaculatus*), 20 (*Ae. aegypti*), 4 (*Ae. sollicitans*), or 10 (*Ae. taeniorhynchus*) repetitions of the test procedure. In the present analysis, entries were weighted by the number of repetitions to obtain the among-subjects mean square on a per-observation basis.

12) Whittemore et al. (1961, Table 2) reported means ($\bar{Y}$) and standard deviations (s) of the protection periods of 2 repellents obtained in paired observations on 10 (n) subjects in tests against *Aedes scapularis* (Rondani) in Texas. The value of Student's t was also reported. In the present study the data were reanalyzed by 2-way (2 treatments × 10 subjects) analysis of variance. Validity of the reanalysis was verified by performing the same operations on a worked exa
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The sums of the squares of the observations in each treatment were obtained by back calculation from *s* as $(n - 1)s^2 + (n\bar{Y})^2/n$. The total sum of squares (total SS) was then obtained by combining the sums of squares so obtained and subtracting the correction term, $C = [\Sigma(n\bar{Y})]^2/\Sigma n$.

The treatment mean square (treatment MS) was obtained from the treatment totals ($n\bar{Y}$) as in the analysis of variance. The error MS was obtained as treatment MS/F, where F is the variance ratio (treatment MS/error MS) obtained as $F = t^2$ (Steel and Torrie 1980:144). Treatment MS and error MS were multiplied by the respective numbers of degrees of freedom to obtain the treatment SS and error SS, and the among-subjects mean square was obtained as (total SS − treatment SS − error SS)/(n − 1).

13) Traub and Elisberg (1962, Table 3, deet) reported the among-subjects standard deviations obtained in 6 determinations of the protection period of deet on 10 subjects in tests against a natural association of mosquitoes in Malaysia. The combined among-subjects standard deviation was obtained as described in Section 3.

14) Wadley (1946:31) reported the among-subjects sum of squares and its associated degrees of freedom in a balanced incomplete block test of 6 repellents on 5 subjects against *Ae. aegypti*. The among-subjects mean square was obtained by dividing the sum of squares by the number of degrees of freedom.

15) Spencer et al. (1977, Table 1) reported among-subjects standard deviations of the protection periods of 4 repellents on 8 subjects in tests against *Ae. aegypti*. Two of the repellents were tested once on each subject, and 2 were tested twice on each subject. The 6 standard deviations were pooled to obtain the combined among-subjects standard deviation.

16) Wiesmann and Lotmar (1949, Table 1) reported the numbers of bites observed 2, 4, 6, 9, 11, and 13 h after application of 2 repellents to 1–8 subjects at a normal rate, a half-normal rate, or as needed for coverage. Tests were conducted against a natural association of mosquitoes in Argentina.

For purposes of the present study, the end point of the protection period was considered to be the midpoint in time between the last recorded negative observation and the 1st recorded positive observation (Rutledge 1988). For example, where 0, 0, 0, 3, 0, and 3 bites were reported at 2, 4, 6, 9, 11, and 13 h, the protection period was considered to be (6 + 9)/2 = 7.5 h.

Protection periods were analyzed as a 2 × 3 (2 repellents × 3 application rates) experimental design with unequal replication (1–8 subjects) using multivariate statistical analysis. The model employed in the analysis included the response variable, PROTECTION PERIOD (quantitative), and 2 explanatory variables, REPELLENT (qualitative) and APPLICATION RATE (qualitative). REPELLENT included 2 classes: epellent 6–2–2 and Kik–Geigy. APPLICATION RATE included 3 classes: normal, half-normal, and as-needed.

In this analysis, the error (within-treatments) mean square represents the among-subjects variance. The estimate is a conservative approximation, because it includes experimental error and is an overestimate.

17) Spencer et al. (1976, Table 3) reported among-subjects standard deviations of the protection periods of 7 repellents on 4–16 subjects in tests against *Ae. aegypti*. Subjects were chosen at random from a pool of 30 males. The standard deviations were pooled to obtain the combined among-subjects standard deviation.

18) Wiesmann and Lotmar (1949:299) reported among-subjects ranges of protection periods of Kik–Geigy repellent obtained in 6 tests against a natural association of mosquitoes in France. The number of subjects employed in the tests was stated to be 5 or 6, but the numbers employed in specific tests were not given. As a conservative approximation, the number of subjects was considered to be 5 in each test. Standard deviations corresponding to the among-subjects ranges were obtained from Table XX of Fisher and Yates (1963) and pooled to obtain the combined among-subjects standard deviation.

19) Spencer and Akers (1976, Table 1) reported among-subjects standard deviations of protection periods of 3 repellents on 4 subjects in tests against *Ae. taeniorhynchus* in Florida. The standard deviations were pooled to obtain the combined among-subjects standard deviation.

Note: Data of Spencer and Akers (1976, Table 2) were not analyzed, because testing of certain (unspecified) repellents was terminated before completion.

20) Rietschel and Spencer (1975, Table) reported among-subjects standard deviations of the protection periods of 0.16 mg/cm² and 0.32 mg/cm² deet on 16 subjects in tests against *Ae. aegypti*. The standard deviations were pooled to obtain the combined among-subjects standard deviation.

21) Skinner et al. (1977, Table 1) reported mean protection periods of deet on 11 subjects in tests against *Ae. aegypti*. The test procedure was repeated 2–8 times on each subject. Subject means were converted to totals, and the among-subjects mean square was computed as in the analysis of variance.

22) Reifenrath and Akers (1981, Table 2) reported the observed protection periods of 4 repellents on 4 subjects in tests against *Anopheles freeborni* Aitken in California. Data for 2 repellents were excluded from the present analysis, because testing of those repellents was terminated before completion. Data for 1-(butylsulfonyl)-hexahydro-1*H*-azepine and triethylene glycol monohexyl ether were analyzed by 2-way (4 subjects × 2 repellents) analysis of variance to obtain the among-subjects mean square.